THE STUDY OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE - CLINICAL PROFILE AND FAMILY SCREENING

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BONAFIDE CERTIFICATE

This is to certify that this dissertation titled **"THE STUDY OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE CLINICAL PROFILE AND FAMILY SCREENING"** is a bonafide work done by **Dr. A.MARI MUTHU** Post Graduate Student, Department of General Medicine, Government Kilpauk Medical College, Chennai-10 under my guidance and supervision in partial fulfillment of regulations of Tamil nadu Dr. M. G. R Medical University, for the award of MD Degree Branch I (General Medicine) during the academic period of from May 2008 - April 2011.

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CONTENTS

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited renal disease (Gabow , PA, Bennet WM, Breuning MH, Peter DJM) ADPKD affect approximately 500000 population in united states and is the most frequent genetic cause of Renal failure in adult accounting for 10% of patient on dialysis in the US (Torra 2008) ADPKD in common hereditary condition caused by mutation of either PKD1, or PKD2 and genetic basis of ADPKD has been clearly established (Scheieren et al 2006) although name describes renal disorder the disease is systemic and includes both cystic and non cystic extra renal abnormalities. These include liver cyst, pancreatic cyst, intracranial and coronary aneurysm, mitral valve prolapse and possibly spontaneous arterial dissection (Demetriou et al 2000)

The main cause of death in ADPKD are Uraemia, atherosclerosis affecting coronary, intracranial and peripheral arteries, sudden rupture of intracranial aneurysm and sepsis (Demetriou et al 2000) ADPKD is phenotypically heterogeneous both between and also within affected families. (Gabow PA, Ravine D Walk, RG Gibson RW et al Kiemberling WJ, Fain PR, Kenyon JB, Goldgar D, Sujansky E, PA.) The inter – familial variability is explained by the well – known genetic heterogeneity with atleast two major genes responsible for ADPKD, and another third putative gene. For both major genes, different mutations are observed in different

families and to this day no single common mutation has been identified.[1, 2,3,4]

Before formal diagnosis of ADPKD has been made, many of the visits to primary care provides like General practioner are related to complication associated with ADPKD, such as hypertension, abdominal pain, and urinary tract infection (UTI) (Torra, 2008). Since clinical symptoms usually begin in the third, fourth, or fifth decade of life, it is important for a primary care provider (PCP) to be aware of this disease and arrange diagnostic imaging or genetic testing to properly diagnose an individual.

It is one of the rare disorder, that involve the kidney it leads to major morbidity and mortality. When we screen the family are can detect disease early and delay the morbidity and mortality due to ADPKD

In this study I am going to evaluate clinical profile of patient attending General Medicine and Nephrology Department and the family screening for the above patients for early diagnosis and treatment, and delay the morbidity, mortality due to ADPKD.

AIM OF THE STUDY

1. Evaluation of clinical profile of Autosomal Dominant Polycystic kidney disease patient attending General Medicine and Nephrology Out Patient / In Patient Department.
2. Family screening of ADPKD patients.

REVIEW OF LITERATURE

Autosomal dominant polycystic kidney disease was described in the nineteenth century in European Medical literature and Sir William Osler had published in the middle of 20th century in USA. Comprehensive study describing the disease was published in 1957 by Dr. O,Z Dalagard reported in his classic doctoral thesis on the inheritance of Polycystic kidney disease (PKD) as an autosomal dominant trait.

Because of its inheritance pattern the children of PKD patient will have a 50% chance of inheriting the disorder. ADPKD occur in worldwide and in all races with prevalence estimated between 1:500 – 1:1000[5] Gabow.

Etiology and pathogenesis of PKD

PKD 1, PKD 2, are expressed in most organs and tissues of the human body. The proteins that are encoded by PKD1 and PKD2, polycystin 1and polycystin 2, seem to function together to regulate the morphologic configuration of epithelial cells[6]. The polycystins are expresses in development as early as the blastocyst stage and are expressed in a broad array of terminally differentiated tissues. The functions of the polycystins have been scrutinized to the greatest extent in epithelial tissue of the kidneys and liver and in vascular smooth muscle. Mutations in either polycystin lead to a clinical phenotype recognized as ADPKD. The hallmarks of this inherited conditions are massively enlarged kidneys caused by the sustained

expansion of innumerable fluid- filled cysts ranging in equivalent size from a pea to a grapefruit. Cyst arise from the nephron and collecting tubules They are seen with lesser frequency in the liver (approximately 80%). Pancreas (approximately 10 %), and arachnoids membrane (approximately 8%).Aneurysms occur in approximately 5% of patients with ADPKD and with higher frequency in those with a family history of aneurysm (approximately 5%) of patients with ADPKD and with higher frequency in those with a family history of aneurysm (approximately 20%). In >60% of patients, hypertension develop before the loss of renal function, and the average age of onset, although highly variable is approximately 30 yr[7-12]. Proteinuria, often used as surrogate marker of disease activity in other kidney disorders, is usually <1 g/d. Proteinuria, observed more frequently in those with large (mean combined renal volume 1190 ml) rather than small (578 ml) renal volumes, is also associated with a greater likelihood of a subsequent loss of renal function.[13]

The renal cysts develop in a tiny fraction of the nephrons (estimated to be much less than 1%)[14]. In ADPKD, each epithelial cell within a renal tubule harbors a germ-line mutation, yet only a tiny fraction of the tubules develop renal cysts. It is currently held that the cells are protected by the allele inherited from the parent without ADPKD. When this allele in inactivated by a somatic event (Mutation or otherwise) within a solitary renal

tubule cell, the cell divides repeatedly until a cyst develops with an aberrant growth program causing endless expansion. The severity of ADPKD is thought to be a direct consequence of the number of times and the frequency with which this cryptogenic process occurs within the kidneys over the life of the patient.

Hyperplasic of renal cyst epithelial cells is unquestioned in this disease; however the rate of cell proliferation is slow in comparison with transformed and malignant neoplastic cells[15]. The hyperplasic cells cause an out- pocketing of the tubule wall, with the formation of a sacular cyst that fills with fluid derived from glomerular filtrate that enters from the afferent tubule segment. Progressive expansion eventually causes most of the emerging cysts to separate from the parent tubule, leaving an isolated sac that fills with fluid by transepithelial secretion. This isolated cyst expands relentlessly as a result of continued proliferation of the mural epithelium together with the transepithelial secretion of NaCl and water into the lumen[16]

The expanding fluid – filled tumor masses elicit secondary and tertiary changes within the renal interstitium evidenced by thickening and lamination of the tubule basement membranes, infiltration of macrophage, and revascularization [17-19]. Fibrosis within the interstitium begins early in the course of the disease. Cellular proliferation and fluid secretion may be accelerated by cAMP and growth factors such as EGF [7,16,20,21]. In summary,

cysts function as autonomous structures and are responsible for progressive kidney enlargement in ADPKD.

Diagnosis of ADPKD

The diagnosis of ADPKD is established primarily by imaging studies of the kidney. Ultrasonography is the procedure of choice in the initial screening, work-up and diagnosis.[22] The clinical diagnostic criteria relying on sonographic finding have a sensitivity of nearly 100 percent. Molecular genetic testing by sequence analysis can be helpful when the imaging results are equivocal and or when a definite diagnosis is required in a younger adult.[23] Gene linkage analysis can be used to determine obligate ADPKD gene carriers, but this method has not gained widespread clinical use and has many practical limitations.[24]

The diagnosis of ADPKD in an individual with positive family history relies on imaging testing counseling should be done be testing. Renal ultrasound is commonly used because of price and safety. As a rule of thumb the minimum requirement for the diagnosis of ADPKD in individuals less than 18 yrs of age 1 cyst, 18-30 yrs of age are 2 cyst (uni / bilateral) at age 30-60yrs more than 4 cysts (2 cyst in each kidney) and age above 60 yrs at least 8 cyst (4 cyst in each kidney)[22]

Cyst development and growth

Many manifestation are directly related to development and enlargement of renal cyst. A study of 241 nonazotemic patients followed prospectively with early MRI examination, The Consortium of Imaging studies to assess the Progression of polycystic kidney disease (CRISP) has provide invaluable information to understand how the cyst develop and grow [25,26] Total kidney volume and cyst volume are increased exponentially. At baseline total kidney volume was 1060 ± 642ml and mean increase over 3yr was 204 ml or 5.3% per year. The rate of change of volume and of Right and left kidney volume were strongly correlated

Renal function abnormalities

Impaired urinary concentrating capacity is common even at early stages.[27] Sixty percent of children can not maximally concentrate the urine. Plasma vasopressin levels are increased. The vasopressin resistant concentrating defect is not explained by reduced C AMP or expression of concentration associated genes. Recent studies suggest that urinary concentrating defect and elevated vasopressin level may contribute to cytogenesis. They may contribute to glomerular hyeprtltration seen in children and young adult[28] and to the development of hypertension and chronic kidney disease defective medullary trapping of ammonia and transfer

to the urine causes by concentrating defect may contribute to the low urine pH values, hypocitric aciduria and predisposition to stone formation.

Reduced renal blood flow is another early functional defect [29] it may be due to changes in internal pressure to neurohumoral to local mediator or intrinsic vascular abnormalities. Mild to moderate persistent proteinuria may be found in a significant number of patients in the middle to late stage of the disease. It is an indicator of progressive diseases[30] patients with proteinuria may also excrete [31] double refractile lipid bodies (oval fat bodies)[31]

Morbidity in ADPKD

Renal hemorrhage and Hematura

Polycystic kidneys are unusually susceptible to traumatic injury, with hemorrhage occurring in approximately 60% of individuals [8,9,19,32,42]. Mild trauma can lead to intrarenal hemorrhage or bleeding into the retroperitoneal space accompanied by intense pain that often requires narcotics for relief[43]. The cysts are associated with excessive angiogenesis evidenced by fragile vessels stretched across their distended walls. When traumatized, these vessels may leak blood into the cyst, causing it to expand rapidly, provoking frightening pain. If bleeding continues, then the cyst may rupture into the collecting system, causing gross hematuria. Alternatively, it may rupture into the subcapsular compartment and eventually dissect through the renal capsule to fill the retroperitoneal space. In massive bleeding, the blood may

reach the skin that covers the flank and abdomen, where it is recognized as subcutaneous ecchymoses (Gray –Turner sign).

Evidence from computed tomography scans indicates that intracyst hemorrhage, manifested as "hyperdense" subcapsular cysts, occurs in >90% of those with ADPKD [44]. Often , dozens of superficial cysts bear the marks of intracyst bleeding. Direct inspection of the "hyperdense" cysts has revealed them to be filled with cellular debris derived from the breakdown of blood products.

Patients with a history of renal hemorrhage evidenced by repeated episodes of gross hematuria have the largest kidneys[8,32] and progress to renal insufficiency faster than those without this history. In a retrospective clinical study, Gabow et al.[8,32] found that male athletes who had ADPKD and participated in constant sports had more hematuric episodes and developed renal insufficiency sooner than those who did not participate. In summary, renal hemorrhage caused by cysts occurs at any age and diminishes the quality of life. Hemorrhage is associated with larger kidneys and accelerated loss of renal function.

Pain

Pain is the most frequent symptom (-60%) reported by adult patients.[45, 46] Acute pain may be associated with renal hemorrhage, passage

of stones, and urinary tract infections. Some patients develop chronic flank pain without identifiable etiology other than the cysts.

Vascular endothelial growth factor (VEGF) produced by the cystic epithelium[47] may promote angiogenesis, hemorrhage into cysts, and gross haematuria. Symptomatic episodes likely underestimate the frequency of cyst hemorrhage because more than 90% of ADPKD patients have hyperdense (CT) of high-signal (MRI) cysts reflecting blood or high protein content. Most Hemorrhages resolve within 2 to 7 days. If symptoms last longer than 1 week or if the initial episode occurs after the age of 50 years, investigation to exclude neoplasm should be undertaken.

Approximately 20% of ADPKD patients have kidney stones usually composed of uric acid and calcium oxalate[48,49]. Metabolic factors include decreased ammonia excretion, low urinary pH, and low urinary citrate concentration. Urinary stasis secondary to the distorted renal anatomy may also play a role. A CT of the abdomen before and following contrast enhancement is the best imaging technique to detect small uric acid stones that may be very faint on plain films with tomograms and to differentiate stones from cyst wall and parenchymal calcifications. Stones may be missed if only a contrast-enhanced CT is obtained.

As in the general population, urinary tract infections affect women more frequently than men. Most are caused by entero bacteriaceae[50]. CT and

MRI are useful to detect complicated cysts and provide anatomic definition, but the findings are not specific for infection. Nuclear imaging (^{67}Ga or^{111} In-labeled leukocyte scans) may be helpful, but false-negative and false-positive results are possible. Cyst aspiration should be considered when the clinical setting and imaging are suggestive and blood and urine cultures are negative.

Renal cell carcinoma (RCC) is a rare cause of pain in ADPKD. It does not occur more frequently than in the general population, but it may present at an earlier age with frequent constitutional symptoms and a higher proportion of sarcomatoid, bilateral, multicentric, and metastatic tumors[51]. A solid mass on ultrasound, speckled calcifications on CT and contrast enhancement, and tumor thrombus and regional lymphadenopathies on CT or MRI should raise the suspiction of carcinoma.

Cosmetic deformation of the Abdomen.

The Kidneys in some Patients enlarge to such an extent that belt and dress sizes must be increased substantially. The additional mass within the abdomen affects posture during standing and walking, which contribute to lower back pain that is separate from the renal pain. Although the effect of cosmetic abdominal distortion on lifestyle and quality of life has not been studied formally, nephrologists who treat large numbers of patients with ADPKD report that many of them find the enlarging abdomen highly

stressful. Huge kidneys may impair diaphragmatic motion enough to disturb sleep. Enlarged kidneys as result of cysts increase the risk that seat belts may cause injury[52]. Patients with greatly enlarged polycystic kidneys complain that seat belts increase pain in normal use. In summary, cosmetic deformation of the abdomen at any age is caused by renal cysts and can adversely affect the quality of life.

Hypertension

Hypertension (BP>140/90) present in approximately 50% of 20 to 34 yrs old patients with ADPKD with normal renal function increases to nearly 100% of patient with ESRD[53] hypertension development is accompanied by reduction in renal blood flow, increased filtration fraction, abnormal renal handing of sodium extensive remodeling of the renal vasculature.

The association between renal size and prevalence of Hypertension supports the hypothesis that stretching and compression of the vascular tree by cyst expansion causes ischiemia and activation of renin angiotensin system[54]. The expression of PCI and PC2 in vascular smooth muscle[55,57] and endothelium[58] along with enhanced vascular smooth muscle contractility[59] and impaired endothelial dependent vasorelaxation[60] suggest that a primary disruption of polycystin function in the vasculature may also play a role in the early development of Hypertension and renal vascular remodeling.

There is strong evidences for local activation of the intrarenal renin angiotensin system. This include reduced Renal blood flow [61-64] shit of immunoreactive renin from juxtaglomerular apparatus to walls of arterioles and small arteries.[65,66] Ectopic Synthesis of Renin[67,68] ACE independent generation of Angiotensin II by a chymase like enzyme[68] other factor proposed to contribute to HT in ADPKD include increased sympathetic nerve activity and plasma endothelin-1 level and insulin resistance[69].

Hypertension has been associated with renal size in several studies of ADPKD[6,10,42,70-79] and normal renal function, the number and volume of renal cysts determined with ultrasound were greatest in those with hypertension[70,73,80,82]. In 165 adult patients with ADPKD, renal volumes determined with ultrasound were significantly greater in those with hypertension than in normotensive patients[10]. Similarly, in a recent cross – sectional study of 241 patients with ADPKD using magnetic resonance imaging (MRI) mean kidney volume was greater in the hypertensive patients than in the normotensive group[21]. Surgical removal of cysts in a large Chinese study of ADPKD patients improved BP control[83,84] in summary, the development of hypertension is associated with the enlargement of ADPKD kidneys secondary to cysts. As explained in these early sections, expanding renal cysts and the vastly enlarged kidneys that the casus provoke serious

morbidities that damage the quality of life long before renal function is diminished.

Renal insufficiency

The development of renal insufficiency is highly variable in ADPKD[9,36,39,41,85] renal failure has been reported in children[86], and conversely individuals with the conditions may live a normal life expectancy without knowing that they have the disease. An early study estimated that approximately 70% of patients with ADPKD would develop renal insufficiency if they survived to age 65[87]. A 1984 report from Canada found that the probability of being alive and not having renal function prognosis is judged. Individuals with mutations in PKD2 develop renal failure approximately 15 yr later than those with PKD1 mutations[9,32,88-91]. However, on clinical inspection , an individual with a PKD2 mutation does not seem physically different from someone with a PKD1 mutation.

Extra renal Manifestations

Polycystic liver disease

Is the most common extrarenal manifestation it is associated with both PKDI and non PKD1 genotypes. PLD also occurs as a genetically distinct disease in the absence of renal cyst. Like ADPKD, ADPLD is genetically heterogeneous with two genes identified (PRKCSH in chromosome 19 and

sec 63 in chromosome 6) accounting for approximately one third of isolated ADPLD cases [92-94]

Prevalence of PLD in MRI in the CRISP study was 58%, 85%, and 94% in 15-24 yrs old, 25-34 yr old and 35-46 yr old participant respectively[72] hepatic cyst are more prevalent, and hepatic cyst volume is larger in women than in men. Women who have multiple pregnancies or who have used and oral contraceptive agent or estrogen replacement therapy have more severe disease suggesting an estrogen effect on hepatic cyst growth[54,95]

Topically PLD is asymptomatic but symptom result from mass effect, infection, hemorrhage mass effect include hepatic venous outflow obstruction, inferior vena cava compression portal vein compression or bile duct compression present on obstructive jaundice.[96]

Cyst in other organs:

Cyst are found in pancreas in approximately 5%, arachinoid in approximately 8%, seminal vesicle in approximately 40%[97-102] seminal vesicle cyst rarely result in infertility[103], Defective sperm motility is another cause of infertility in ADPKD[104], pancreas cyst are almost asymptomatic arachinoid membrane cyst are asymptomatice but may increase the risk of subdural haematoma.[105], spinal meningeal diverticula may occur with

increased frequency and rarely present with intracranial hypotension due to cerebrospinal fluid leak[106], ovarian cyst are not associated with ADPKD.

Vascular manifestations:

These in clude ICA and dolichoectasis, thoracic aortic and cervicocephalic artery dissection and coronary artery aneurysm they are caused by alteration in the vasculature directly linked to mutation in PKD1, or PKD2. PC1, PC2, are expressed in vascular smooth muscle cell intracerebral artery aneurysm occur in approximately by 6% of patient with negative family history and 16% of those with positive family History of aneurysm[107], Rupture carries 35 to 50% risk of combined morbidity and mortality.[108],

Cardiac manifestations

Mitral valve prolopse observed by echocardiogram is the most common valvular abnormality found in 25% of patients[109,110] aortic insuffiency may occur in Association with dilation of the aortic root[111].

Diverticular disease:

Colonic diverticulosis and diverticulitis are more common in ESRD. Patients with ADPKD than in those with other renal disease. Whether this increased risk extend to patient before the onset of ESRD is uncertain[112]. There have been reports of extra colonic diverticular disease[113].

MATERIALS AND METHODS

The present study titled "study of Autosomal Dominant polycystic kidney disease - clinical profile and family screening" was carried out in the department of General and Nephrology Department, Kilpauk Medical College Hospital Chennai – 10.

Study Design

- Descriptive study
- Family screening study

Period of study:

January 2010 to October 2010

Study Sample.

- 30 Index cases

Materials

- Questionnaires
- Blood pressure
- Complete blood count
- Urine Routine examination
- Urine Culture and sensitivity
- Urine Spot PCR
- Random Blood sugar
- Blood urea

- Serum Creatinine
- Serum Calcium
- Serum phosphate
- Serum uric acid
- ECG
- Chest X –ray (PA View)
- Echo cardiogram
- Ultrasonography
- CT (Computed tomography)

Study Group

The study group included persons with ADPKD and newly detected ADPKD patient by family screening method attending General Medicine and Nephrology Out patient / In patient was included in this study.

Inclusion Criteria

1. Known ADPKD patients (index case) and newly detected ADPKD (Screened case) patients who gave informed consent to participate in the study.
2. ADPKD with CKD all stages.

Exclusion Criteria

- Patient unwilling for study.
- Age below 14 yr not included in the study.

(Paediatrics age group patient not included, and under the age of 14% ultrasound is only correct in 50%)

All the patient in the study group were selected without any bias for sex, Age group, above 14 yrs. With all the stages of CKD was included. A through history was recorded with particular emphasis on symptom of ADPKD. The presence of extra renal symptom was also included family screening was done by enquire about renal symptom, doing ultrasound examination and for doubtful case CT abdomen was done.

A through General and systemic examination was carried. Echo cardiogram was done to rule out mitral valve prolapse, Aortic Regurgitation. CT abdomen also done to rule out pancreatic cyst, fallopian tube cyst, splenic cyst, and ovarian cyst.

The diagnosis of ADPKD was confirmed when the presence of bilateral renal cysts, totaling 5 or more, were visualized by ultrasonography or computed tomography, with positive family history or extra renal mani festatiosn such as hepatic cysts, aneurysms of cerebral arteries, and cysts of the pancreases (welling and Grantham, 1991). All patients past and family histories were reevaluated and charts and ultrasonography report were reviewed retrospectively.

Patients age at initial diagnosis, sex, past and family histories, symptoms and signs, laboratory data, electrocardiogram, abdominal or other

organ ultrasonography, computed tomography (CT), echocardiography, and other study data brain CT scan were analyzed.

Blood sugar

It is estimated by glucose oxidase peroxidase method

Fasting glucose ≥ 126 mgs/dl

Random Blood Sugar ≥ 200 mgs/ dl

patients with symptom

were taken as diabetes mellitus,

FPG = 100 – 125mgs/dl considered as IGT (impaired glucose tolerance).

Renal Function Test

Blood urea

Blood urea in this study was estimated by using DAM method (Diacetyl Monoxime) The normal value of which being 20-40 mgs /dl

Serum creatinine

Serum creatinine was estimated by using modified Jaffe reaction method, alkaline pictrate method. The value of >1.5 mg in male and female and suggestive of renal impairment.

Serum Electrolytes

Serum sodium and potassium were estimated by using flame photometer method.

Urine Analysis

Urine sample is collected for urine routine analysis which include sugar, protein , cytology and urinary sediments.

Urine sugar is estimated by strip method, and Benizidine test

Urine Albumin is estimated by heat coagulation method

Urine Deposit - By direct microscopy examination.

Urine spot PCR:

Urine sample is collected to estimate protein creatinine ratio. Sulfosalicylic precipitaton method, used for protein and creatinine estimation, latex turdity method also used.

Complete blood count

Total count, Differtential count done by smear method to rule out infection in UTI,

Hb - shallish method, to rule out anemia in CKD

ESR – Wintrobe method

Urine culture and sensitivity

It was done by using plate method to rule out organism and sensitivity.

Serum calcium, uric acid, Phosphate

Serum calcium was done by flame photometer method Serum uric acid was done by Uricase POD method, Serum phosphate was done by UV end point method to assess the CKD stage.

Creatinine clearance (Cl_{cr})

If the serum creatinine is stable, the Glomemlar Filtration Rate (GFR) can be estimated by using Cockcroft Gault formula

$$Cl_{cr}\ m1/mt = \frac{140 - age \times IBW\ in\ kg}{72 \times Serum\ Creatinine\ (mg/dl)}$$

X0.85 for women

Glomemlar Filtration Rate used to asses chronic kidney disease (CKD) stages

CKD (Chronic Kidney Disease) stage

NKF Definition of Chronic Kidney Disease

- Kidney damage for three or more months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifested by pathologic abnormalities or markers of kidney damage, including abnormalities in the composition of the blood or urine or abnormalities in imaging tests

- GFR <60 mL per minute per 1.73 m2 for three months or more, with or without kidney damage
- As per definition ADPKD consider as CKD

Stage	GFR ml/mt /1.73 m^2
O	90[a]
1	≥ 90[b]
2	60-89
3	30-59
4	15-29
5	<15

a- With risk factor

b- With demonstrated kidney damage (e.g persistent proterinuria, abnormal urine sediment, and abnormal urine / blood biochemistry abnormal imaging studies.

(Sources modified from National Kidney foundation, K/DOQI Clinical practice guideline for chronic kidney Disease evaluation, classification, stratification Am J Kidney Dis 39 Supp, 2002)

Ultrasonography

The cyst in the kidney (uni / bilateral / multiple) and cyst in other organ like spleen, ovary, seminal vesicle, uterine tube were visualised by

using a Larsen turbo ltd, sonata pus Ultrasonogram in GKMCH Department of radiology.

By Ultrasonography cysts are round or oval, echo lucent, thin walled, clearly delineated structures with smooth contours exhibiting sharply demarcated posterior walls and sound wave amplification behind the cysts as well as lateral extinction of the sound wave (lateral shadowing). if cysts are solitary or infrequent, they must be distinguished from haematoma or abscess, occasionally also from malignancy, particularly lymphoma.

The sensitivity of Ultrasonography to detect renal cysts in carrier of the ADPKD trait depends first on the quality of the Ultrasonography machine (with outdated machines assessments may not be reliable) and second on the age of the porosities. as a rule of thumb, in individuals aged 30 years, cysts are demonstrable by ultrasound in approximately 68% and above 30 years , of age in approximately 89% of carriers of the genetic trait[75]

Computed Tomography

Computed tomography (CT) scanning is a sensitive as Ultrasound in the detection of cystic disease, although problems may arise with smaller cysts. CT scanning appears to be more specific than Sonography in differentiating an obstructed renal pelvis from a Parapelvic cyst. It also seems to be superior to Ultrasonographic images in helping assess

retroperitoneal rupture of a cyst and Perinephric extension of blood or pus from an infected cyst.[62]

Stages of Hypertension (According To Jnc Vii)

Stages	Systolic BP	Diastolic BP
Normal	Less than 120	Less than 80
Pre-hypertension	120 - 139 systolic	80 - 89 diastolic
Stage 1	140 - 159 systolic	90 - 99 diastolic
Stage 2	160 - 179 systolic	100 - 109 diastolic

RESULTS AND ANALYSIS

The present study titled a study of "Autosomal dominant polycystic kidney disease - clinical profile and family screening" was undertaken in the Department of General Medicine and Nephrology, Kilpauk medical college hospital Chennai- 10. over the period of 10 months from January 2010 to October 2010.

The study sample included 30 ADPKD patient (index case) attending as outpatient / inpatient in Dept of General Medicine and Nephrology and 15 cases detected from while doing family screening for that Index case. 20 families were screened out of 30 families. In this 20 families 11 families were positive, 9 families were negative. In this 11 families 15 cases were detected, from 75 screened person.

RESULTS

1. In this study, age of patients attending OP/ IP is ranged from 27-67 yrs in index cases, 13-42 yr in screened cases (Table 1)
2. The Maximum Numbers of age group patients attending OP/IP in the age of 51-60 years. (Table 1)
3. Male to female ratio was 15:15 in Index case, 4:11 in Screened case. (Table 2).
4. In this study 19 patients presented with pain abdomen, 10 patients had UTI, 3 patients had haematuria, Renal calculus, 4 patients had Uraemic symptom, 5 patients had palpable mass. (Table 3)
5. ADPKD was diagnosed by (a) Renal symptom like pain abdomen, palpable mass, gross haematuria, symptoms of UTI – 19 patients (63.4%). (b) by Incidental finding – 7 patients (23.7%) (c) by Uraemic symptoms 4 patients (13.3%) (Table 4)
6. Hypertension was found in 21 patients (70%) in Index cases, 1 patient in Screened case (6.6%). In 9 patients serum creatinine was <1.2 mg/dl. This 9 patients had HT. In 21 patients serum creatinine was ≥1.2 mg/dl. In the 21 patients 12 patients had HT (Table 6)
7. All the subject undergone abdominal ultrasonography more than once 7 patient had Undergone abdominal computed tomography. Extrarenal mani festation was found to be in 11 patients out of 30

patients out of 30 patients in index cases, 5 patients out of 15 patients in screened cases (table 7) and their frequencies are shown (table 8) gastro intestinal manifestation include hepatic cyst in 4 cases (13.3%), pancreatic cyst 1 case (3.3%). 15 female patient out of 30 patient undergone pelvic Ultrasonogrphy, ovarian cyst found to be in 2 patients (13.3%) and uterine cyst found to be in 1patient (6.6%). Seminal vesicle cyst found in 1 patient (6.6%). All patient undergone echocardiogram done as a routine exam. Clinically three patient had mid systolic click, in this 2 patient found to be MVP (mitral valve prolapse) in echocardiogram. 4 patients c/o chronic headache for that patient undergone ct brain (plain) nothing abnormality detected. MRI A, MRI V is the ideal investigation for this case, because of affordability MRI A, MRI V not done.

8. Anaemia was found to be in 9 patients in Index cases and 2 patients in Screened cases. Oedema was found to be in 2 patients in Index cases (Table 12)
9. Mean age at first diagnosis was 40.5 ±18.2 (Mean ±SD) years, in Index case and in 15 cases (50%) first diagnosis of ADPKD has been made in patient 40's and 50's.

10. 5 patients presented with CKD stage I, 9 patients presented with CKD stage II, 7 patients presented with CKD stage III and IV, 2 patients presented with CKD stage V (Table 8) in Index cases.
11. 21 patients on regular follow up in Index cases, 4 patients on regular follow up in Screened cases show in (Table 12). Urine spot PCR was raised in 6 (20%) patients in Index cases.
12. In this study 20 families (out of 30 families) attended screening shown in (Table 13). In this 20 families, 11 families were found to be positive, 9 families were negative (Table 14)
13. Urine spot PCR was increased in 6 patients (20%) in Index cases.

Table - 1

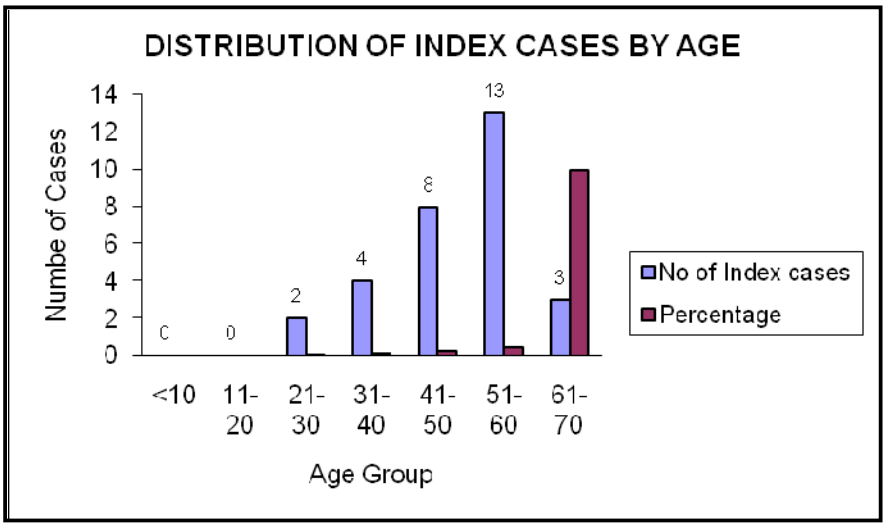
DISTRIBUTION OF CASES BY AGE

S.No	Age Group	No of Index cases	Percentage	No of Screened cases	Percentage
1	<10	0	0	0	0
2	11-20	0	-	5/15	33.3%
3	21-30	2/30	6.7%	6/15	40%
4	31-40	4/30	13.3%	4/15	26.7%
5	41-50	8/30	26.6%	0	0
6	51-60	13/30	43%	0	0
7	61-70	3/30	10	0	0

The mean age of distribution of case is this

Study was 50.03 ±11.4 (Mean ± SD), 27-67 (Range) in Index Case.

(28.2 ± 8.5) (Mean ± SD), 13- 42 (Range) in Screened case.


DISTRIBUTION OF INDEX CASES BY AGE
Numbe of Cases
14
12
10
8
6
4
2
0
0
0
2
4
8
13
3
<10
11-20
21-30
31-40
41-50
51-60
61-70
Age Group
No of Index cases
Percentage

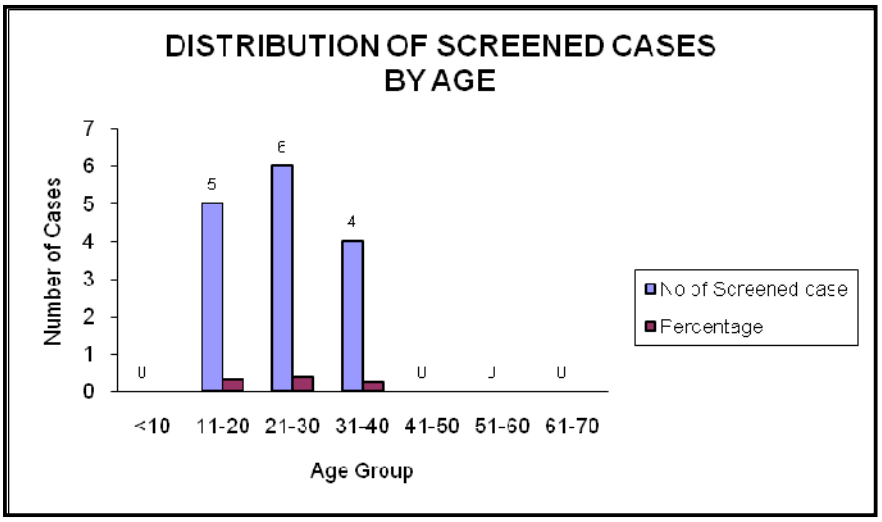
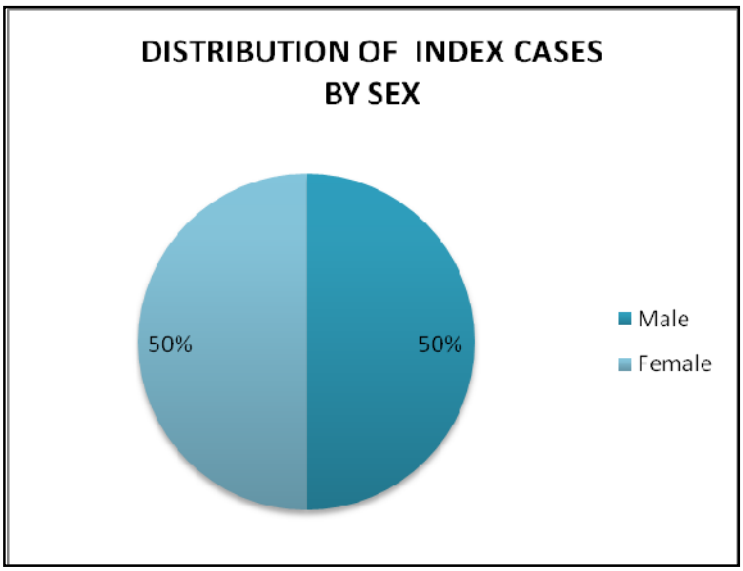

DISTRIBUTION OF SCREENED CASES BY AGE
Number of Cases
7
6
5
4
3
2
1
0
0
5
6
4
0
0
0
<10
11-20
21-30
31-40
41-50
51-60
61-70
Age Group
No of Screened case
Percentage

Table - 2

DISTRIBUTION OF CASES BY SEX

S.No	Gender	No of Index cases	Percentage	No of Screened cases	Percentage
1	Male	15/30	50	4/15	26.7%
2	Female	15/30	50	11/15	73.3%

Male and female was equal distribution in Index cases 15:15 (M:F) where as in Screened cases it was 4:11 (M.F). Most of the cases were female in screened cases.


DISTRIBUTION OF INDEX CASES
BY SEX
50%
50%
Male
Female

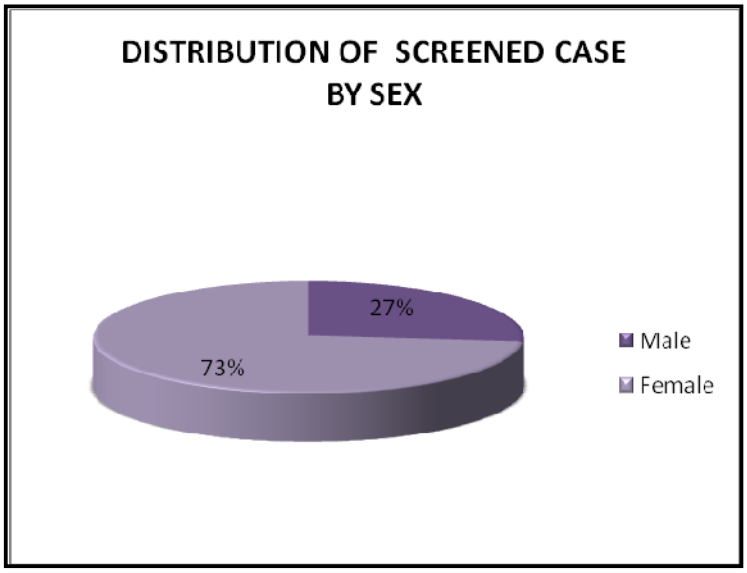
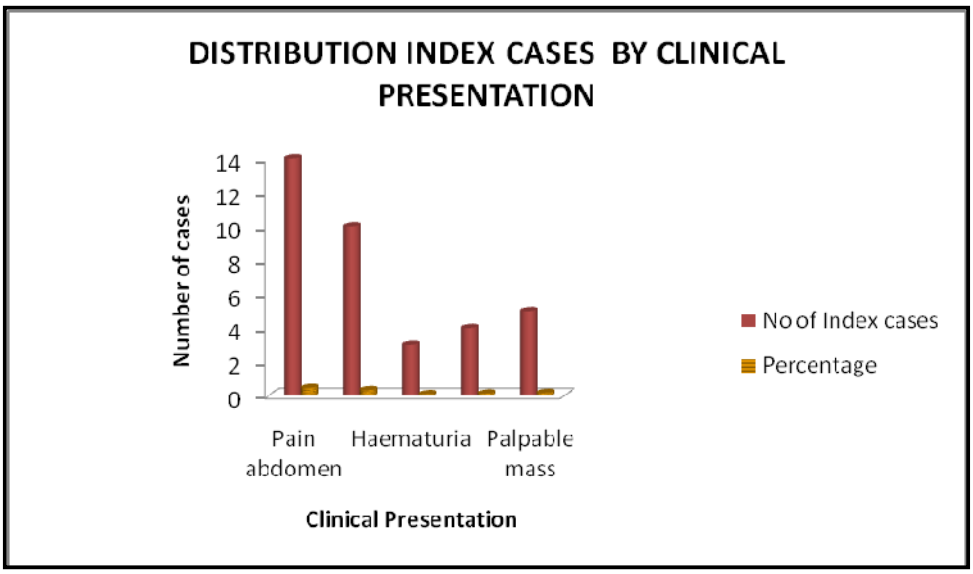

DISTRIBUTION OF SCREENED CASE
BY SEX
27%
73%
Male
Female

Table - 3

DISTRIBUTION CASES BY CLINICAL PRESENTATION

S.No	Clinical Presentation	No of Index cases	Percentage	No of Screened cases	Percentage
1	Pain abdomen	14/30	46.6%	2/15	13.3%
2	UTI	10/30	33.3%	2/15	13.35
3	Haematuria	3/30	10%	-	-
4	Uraemic Symptoms	4/30	13.3%	-	-
5	Palpable mass	5/30	16.6%	-	-

Most of the cases had Pain abdomen in Index cases (14/30) UTI is the next most clinical presentation, 9 patients had UTI. In this 9 patient, 6 patients urine culture and sensitirity found to be positive. In this 6 patients, 5 patients urine shows E. coli growth. 1 patient urine shows klessiella growth.


DISTRIBUTION INDEX CASES BY CLINICAL PRESENTATION
Number of cases
14
12
10
8
6
4
2
0
Pain abdomen
Haematuria
Palpable mass
Clinical Presentation
No of Index cases
Percentage

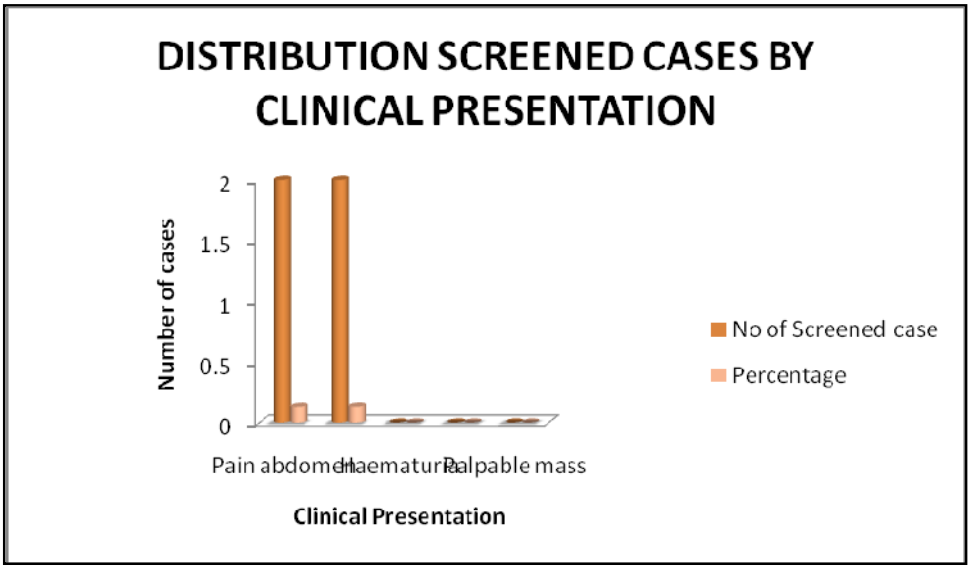

DISTRIBUTION SCREENED CASES BY CLINICAL PRESENTATION
Number of cases
2
1.5
1
0.5
0
Pain abdomen
Haematuria
Palpable mass
Clinical Presentation
No of Screened case
Percentage

Table - 4

DISTRIBUTION OF CASES BY ROUTE OF DIAGNOSIS

(INDEX CASES)

S. No	Route of diagnosis	No of Cases	Percentage
1	Renal symptoms	19/30	63.4%
2	Uraemic symptoms	4/30	13.3%
3	Incidental Finding (Routine Checkup, Master Health Checkup, Infertility Checkup, Antenatal Checkup, Post Menopausal Checkup)	7/30	23.3%

Most of the cases were diagnosed by Renal symptom like Pain abdomen, palpable mass, haematuria, symptom of Renal Infection, stone and nocturia of about 19 patients (63.4%), By uraemic symptom 4 patients (13.3). By incidental finding like Routine check up. Master health checkup. Infertility checkup, antenatal checkup,post menopausal checkup 7 patients (23.3%).

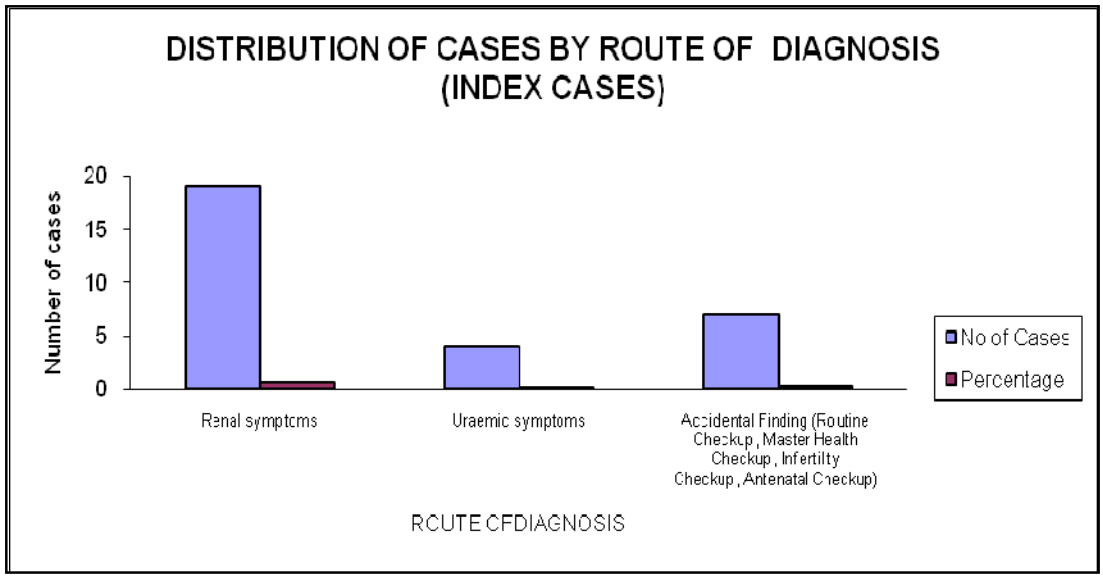
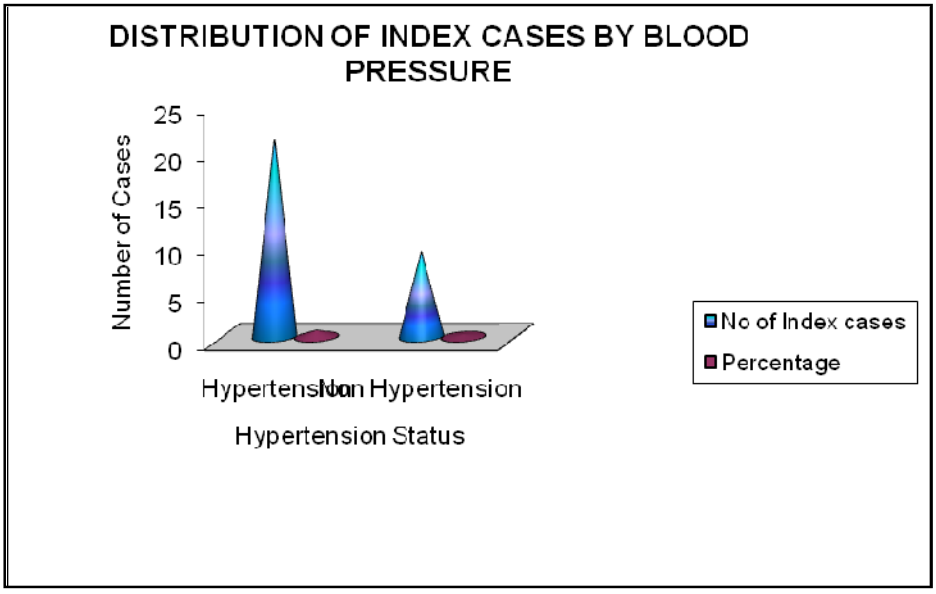

DISTRIBUTION OF CASES BY ROUTE OF DIAGNOSIS
(INDEX CASES)
Number of cases
20
15
10
5
0
Renal symptoms
Uraemic symptoms
Accidental Finding (Routine Checkup, Master Health Checkup, Infertilty Checkup, Antenatal Checkup)
No of Cases
Percentage
ROUTE OFDIAGNOSIS

Table - 5

DISTRIBUTION OF CASES BY BLOOD PRESSURE

S. No	Blood Pressure	No of Index cases	Percentage	No of Screened cases	Percentage
1	Hypertension	21/30	70%	1/15	6.6%
2	Non Hypertension	9/30	30%	14/15	93.4

Hypertension was found to be in 21(70%) patient in Index cases, 1 patient in screened cases. In this 21 patients 9 patients were male, 12 patient were female.


DISTRIBUTION OF INDEX CASES BY BLOOD PRESSURE
Number of Cases
25
20
15
10
5
0
Hypertension
Non Hypertension
Hypertension Status
No of Index cases
Percentage

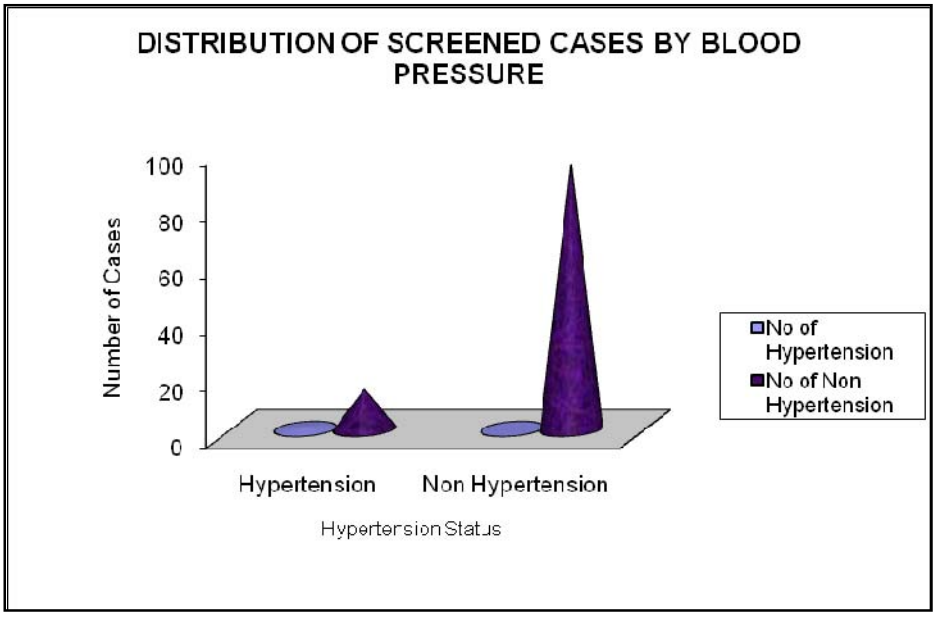

DISTRIBUTION OF SCREENED CASES BY BLOOD PRESSURE
Number of Cases
100
80
60
40
20
0
Hypertension
Non Hypertension
Hypertension Status
No of Hypertension
No of Non Hypertension

Table - 6

DISTRIBUTION OF CASES BY HYPERTENSION VERSUS SERUM CREATININE

S. No	Hypertension / Serum Creatinine <1.2 mg /dl	%	Hypertension / Serum Creatinine ≥ 1.2 mg/dl	%
1	9/9	100%	12/21	57.14%

Serum creetinine was <1.2 mg/dl in 9 patients, this 9 patients had hypertension, where as in 21 patients serum creatinne was ≥ 1.2 gm/dl. In this 21 patients 12 patients had hypertension

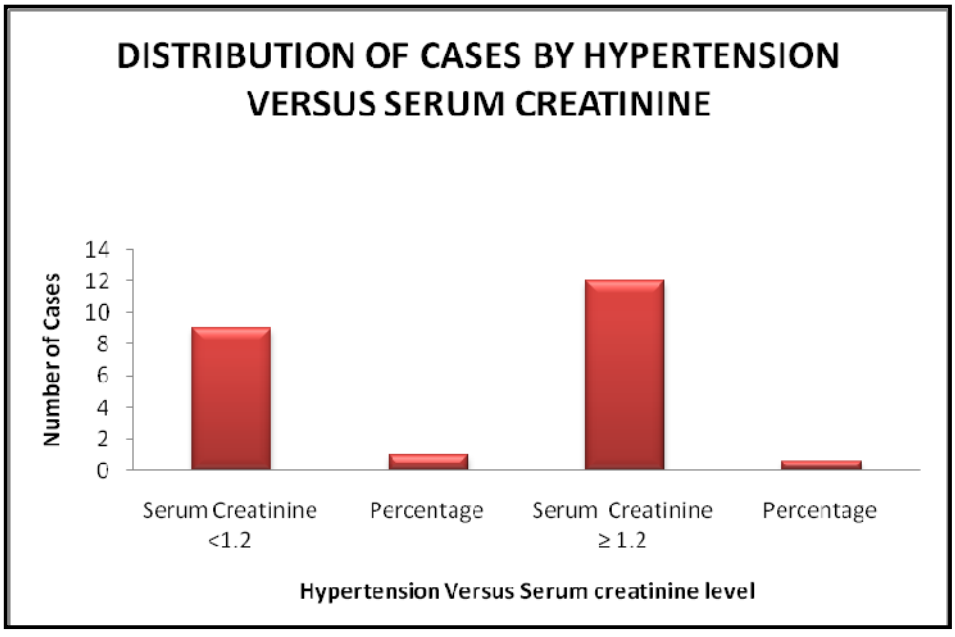
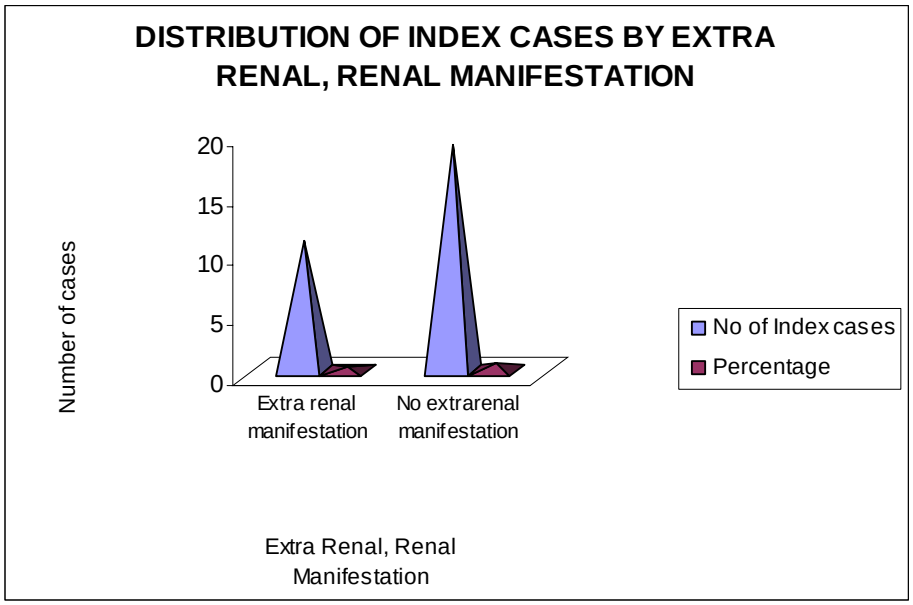


Table - 7

DISTRIBUTION OF CASES BY EXTRA RENAL, RENAL MANIFESTATION

S. No	Extra Renal, Renal Manifestation	No of Index cases	Percentage	No of Screened cases	Percentage
1	Extra renal manifestation	11/30	36.7%	5/15	33.3%
2	No extrarenal manifestation	19/30	63.3%	10/15	66.7%

Extra renal manifestation was found to be in 11 patients (36.7%) in index cases, where as in screened cases it was found to be 4 patients (33.3%).


DISTRIBUTION OF INDEX CASES BY EXTRA RENAL, RENAL MANIFESTATION
Number of cases
20
15
10
5
0
Extra renal manifestation
No extrarenal manifestation
No of Index cases
Percentage
Extra Renal, Renal Manifestation

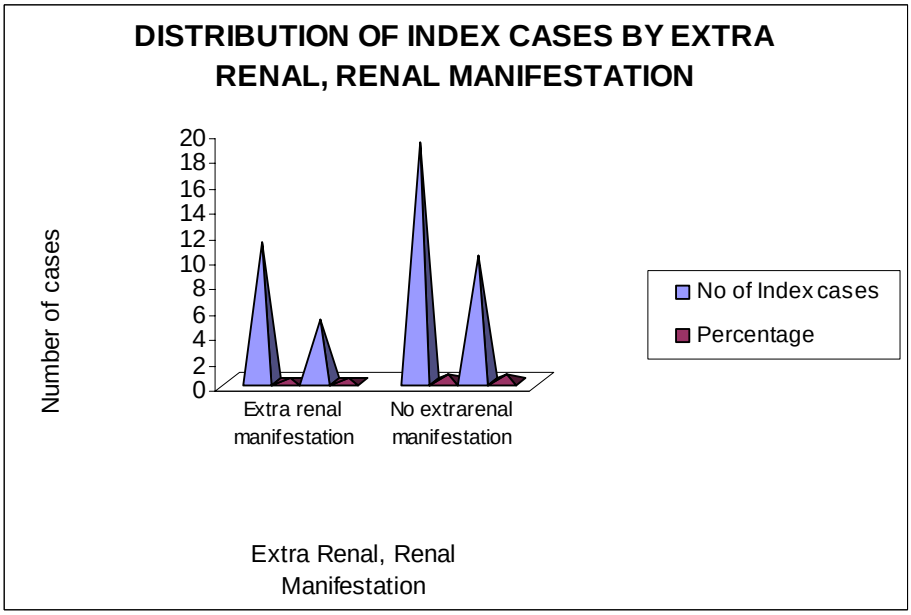
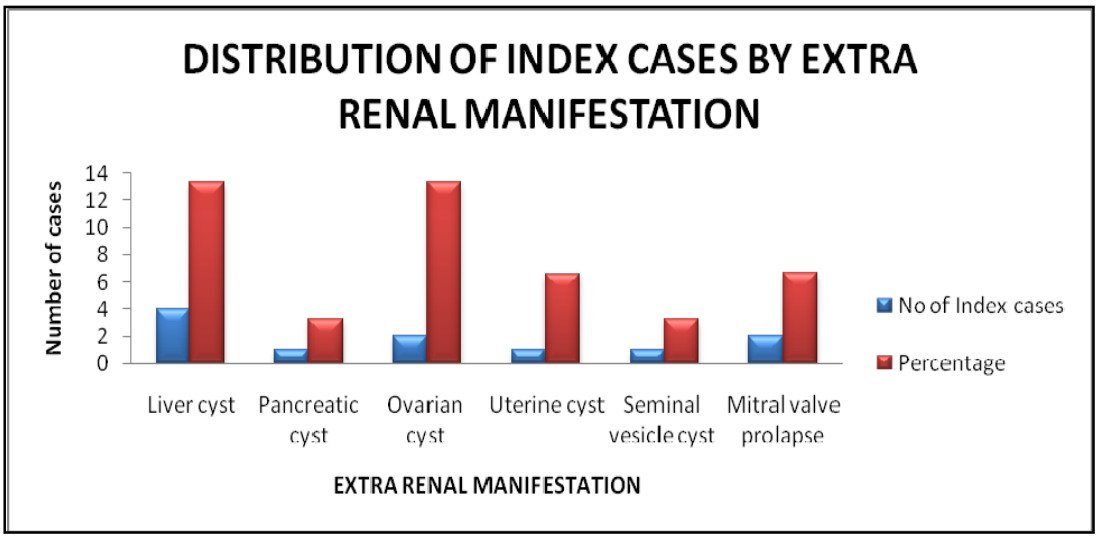

DISTRIBUTION OF INDEX CASES BY EXTRA RENAL, RENAL MANIFESTATION
Number of cases
20
18
16
14
12
10
8
6
4
2
0
Extra renal manifestation
No extrarenal manifestation
No of Index cases
Percentage
Extra Renal, Renal Manifestation

Table - 8

Distribution of cases by Extra renal manifestation

S. No	Extra renal Manifestation	No of Index cases	Percentage	No of Screened cases	Percentage
1	Liver cyst	4/30	13.3	2/15	13.3
2	Pancreatic cyst	1/30	3.3	-	
3	Ovarian cyst	2/15	13.3	1/11	9.1
4	Uterine cyst	1/15	6.6	1/11	9.1
5	Seminal vesicle cyst	1/15	6.6	-	
6	Mitral valve prolapse (MVP)	2/30	6.7	1/15	6.6

In Index cases Liver cyst was found to be in 4 patients (13.3%), pancreatic cyst in 1 patient (3.3%), ovarian cysts in 2 patient (2/15) (13.3%) uterine cyst in 1 patient (6.6%) MVP in 2 patients 6.6%) where as in screened cases liver cyst in 2 patients (13.3%) ovarian cyst in 1 patient (1/11) (9.1%) uterine cyst in 1 patient 1/11 (9.1%). MVP in 1 patient.(6.6%).


DISTRIBUTION OF INDEX CASES BY EXTRA RENAL MANIFESTATION
Number of cases
14
12
10
8
6
4
2
0
Liver cyst
Pancreatic cyst
Ovarian cyst
Uterine cyst
Seminal vesicle cyst
Mitral valve prolapse
No of Index cases
Percentage
EXTRA RENAL MANIFESTATION

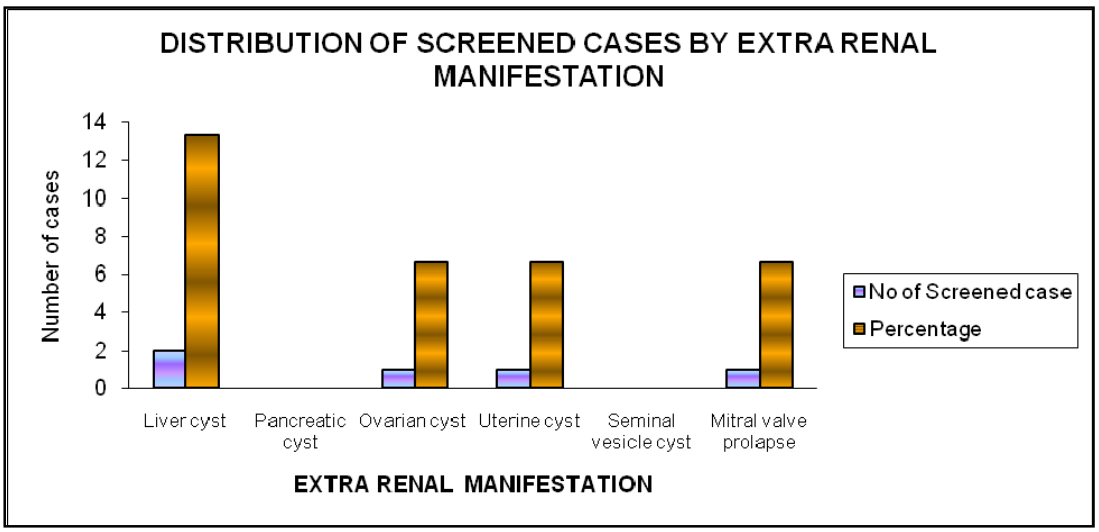

DISTRIBUTION OF SCREENED CASES BY EXTRA RENAL MANIFESTATION
Number of cases
14
12
10
8
6
4
2
0
Liver cyst
Pancreatic cyst
Ovarian cyst
Uterine cyst
Seminal vesicle cyst
Mitral valve prolapse
No of Screened case
Percentage
EXTRA RENAL MANIFESTATION

Table - 9

DISTRIBUTION OF CASES BY ANAEMIA/ OEDEMA

S. No	Anaemia, oedema distribution	No of Index cases	Percentage	No of Screened cases	Percentage
1	Anaemia	9/30	30%	2/15	13.3%
2	Oedema	3/30	10%	-	-

Anaemia was found to be in 9 patients (9/30) 30% Oedema was found to be in 3 patients (3/30) 10% in Index cases, where as in screened cases anaemia was found to be 2 patients 2/15 (13.3%).

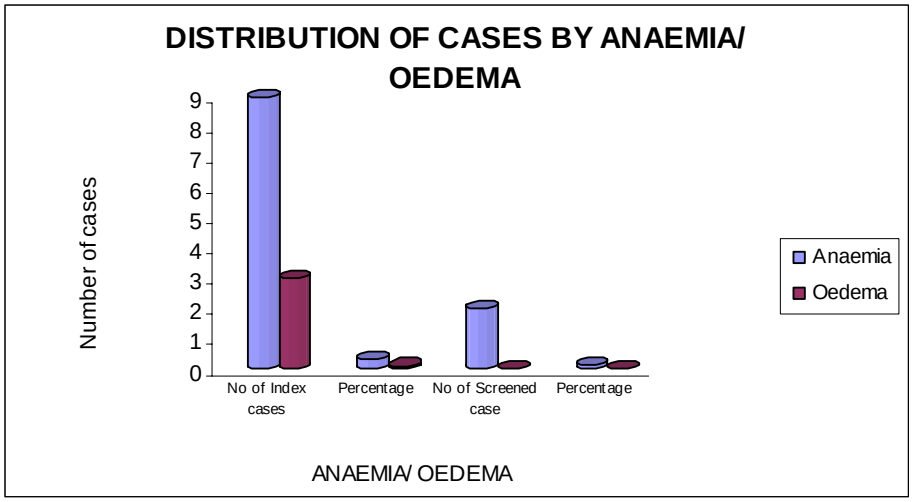
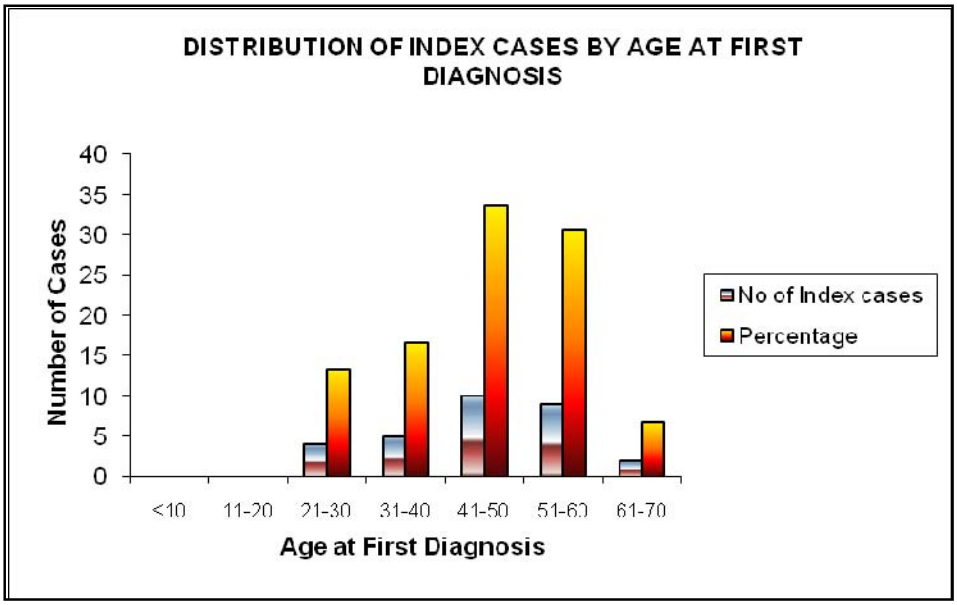


Table - 10

DISTRIBUTION OF CASES BY AGE AT FIRST DIAGNOSIS

S. No	Age group	No of Index cases	Percentage	No of Screened cases	Percentage
1	<10	0	0	0	0
2	11-20	0	0	5/15	33.3
3	21-30	4/30	13.3	6/15	40
4	31-40	5/30	16.6	4/15	26.7
5	51-60	9/30	30.7	0	0
6	61-70	2/30	6.7	0	0

The mean age at first diagnosis in this study was 40.9 ± 18.2 (Mean ±SD) Range (24-65) in Index cases, where as in screened it was 24.9 ±7.9 (mean ±SD) Range (13-27).


DISTRIBUTION OF INDEX CASES BY AGE AT FIRST DIAGNOSIS
Number of Cases
40
35
30
25
20
15
10
5
0
<10
11-20
21-30
31-40
41-50
51-60
61-70
Age at First Diagnosis
No of Index cases
Percentage

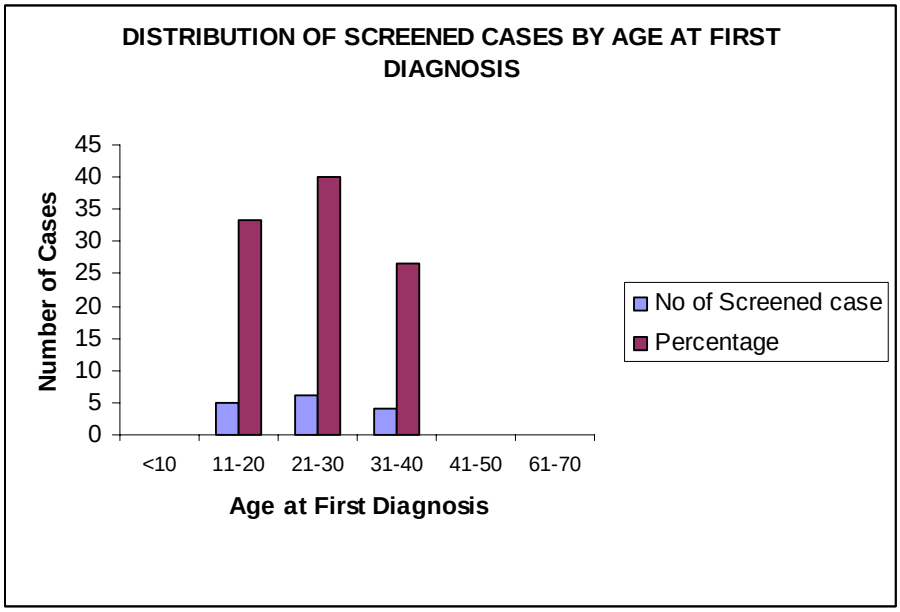
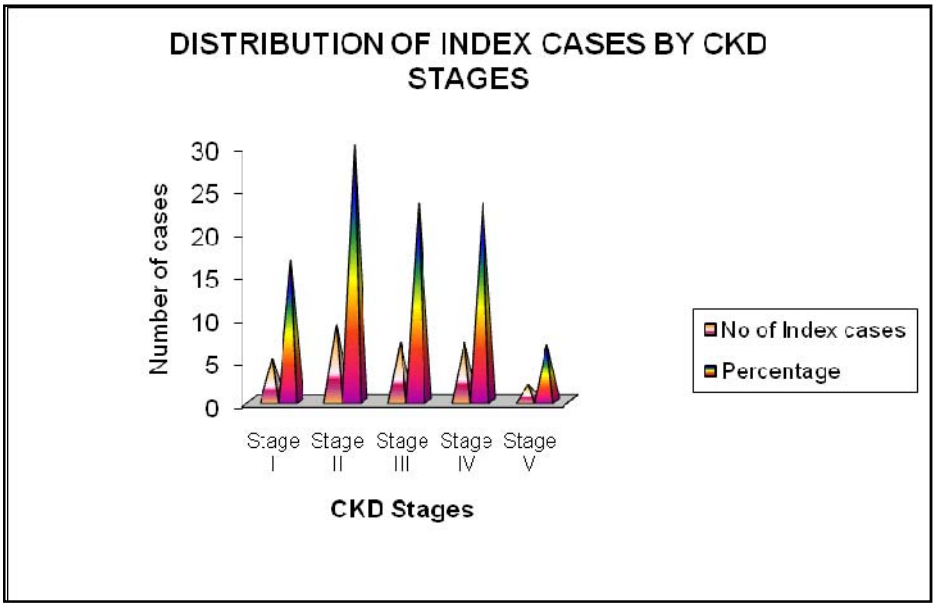

DISTRIBUTION OF SCREENED CASES BY AGE AT FIRST DIAGNOSIS
Number of Cases
45
40
35
30
25
20
15
10
5
0
<10
11-20
21-30
31-40
41-50
61-70
Age at First Diagnosis
No of Screened case
Percentage

Table - 11

DISTRIBUTION OF CASES BY CKD STAGES BASED ON COCK CROFT GAULT FORMULA

S. No	Stages	No of Index cases	Percentage	No of Screened cases	Percentage
1	Stage I	5/30	16.6	15/15	100
2	Stage II	9/30	30	0	0
3	Stage III	7/30	23.3	0	0
4	Stage IV	7/30	23.3	0	0
5	Stage V	2/30	6.7	0	0

In this study most of the case found to be CKD stage II, III, IV in Index cases. where as in screened cases all cases found to be CKD stage I.


DISTRIBUTION OF INDEX CASES BY CKD STAGES
Number of cases
30
25
20
15
10
5
0
Stage I
Stage II
Stage III
Stage IV
Stage V
CKD Stages
No of Index cases
Percentage

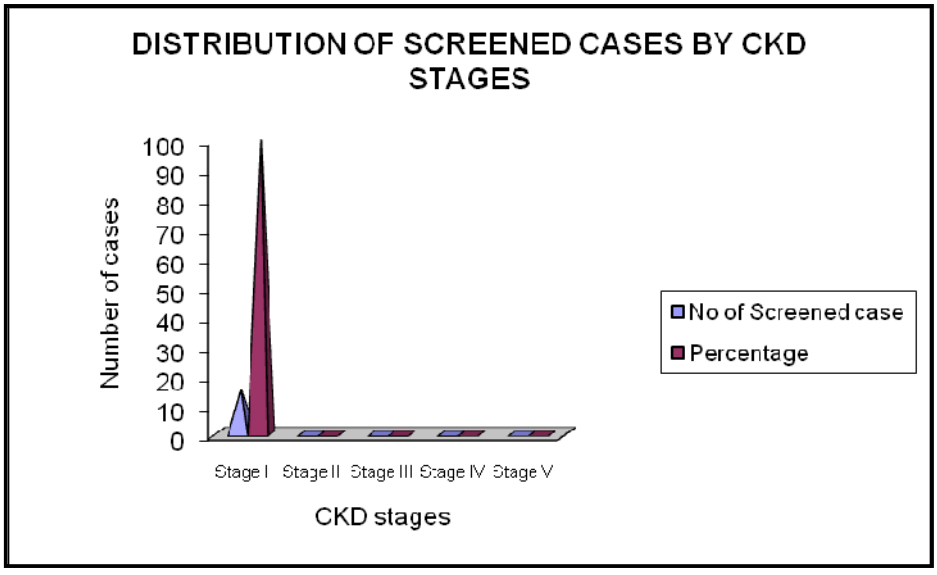
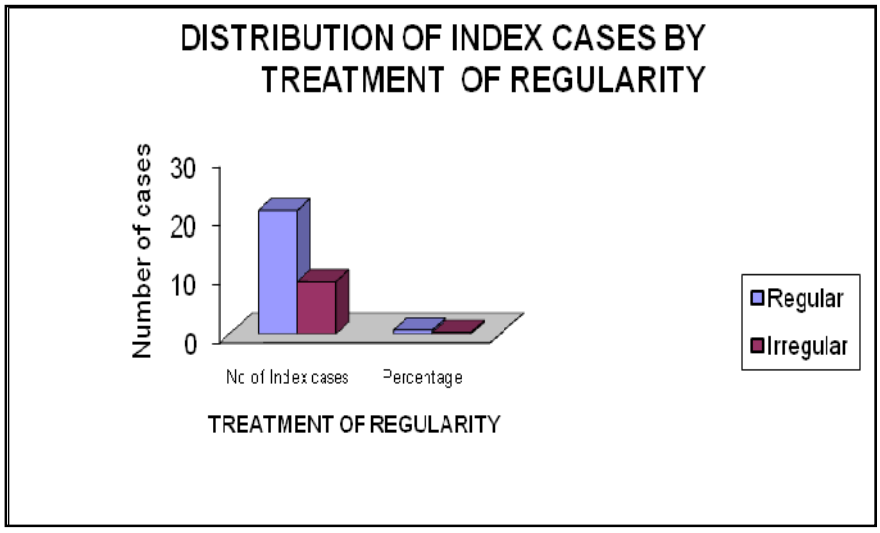

DISTRIBUTION OF SCREENED CASES BY CKD STAGES
Number of cases
100
90
80
70
60
50
40
30
20
10
0
Stage I
Stage II
Stage III
Stage IV
Stage V
CKD stages
No of Screened case
Percentage

Table - 12

DISTRIBUTION OF CASES BY TREATMENT OF REGULARITY

S. No	Treatment of regularity	No of Index cases	Percentage	No of Screened case	Percentage
1	Regular	21/30	70%	4/15	26.7
2	Irregular	9/30	30%	11/15	73.3

In this study 21 cases on regular follow–up. 9 case not on regular follow up in Index cases, where as in screened cases 4 cases on regular follow – up 11 cases not on regular follow up.


DISTRIBUTION OF INDEX CASES BY TREATMENT OF REGULARITY
Number of cases
30
20
10
0
Nc of Index cases
Percentage
TREATMENT OF REGULARITY
Regular
Irregular

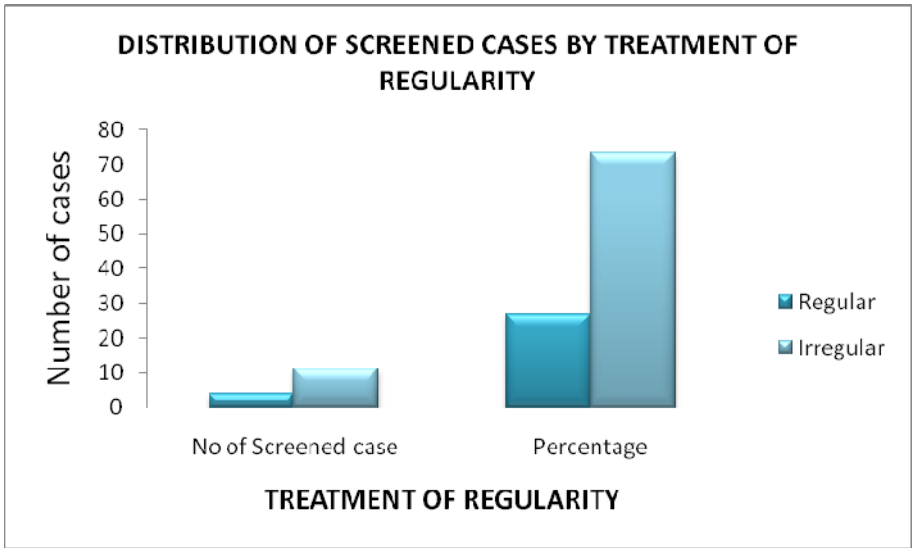

DISTRIBUTION OF SCREENED CASES BY TREATMENT OF REGULARITY
Number of cases
80
70
60
50
40
30
20
10
0
No of Screened case
Percentage
TREATMENT OF REGULARITY
Regular
Irregular

Table - 13

DISTRIBUTION OF CASES BY FAMILY SCREENING

S. No	Family screening details	No of Index cases	Percentage
1	No. of family attended screening	20/30	66.6
2	No. of family not attended screening	10/30	33.4

In this study 20 families (66.6%) attended screening, 10 families (33.4%) not attended screening. This is because of social stigma about Renal disease and lack of awareness about treatment modalities.

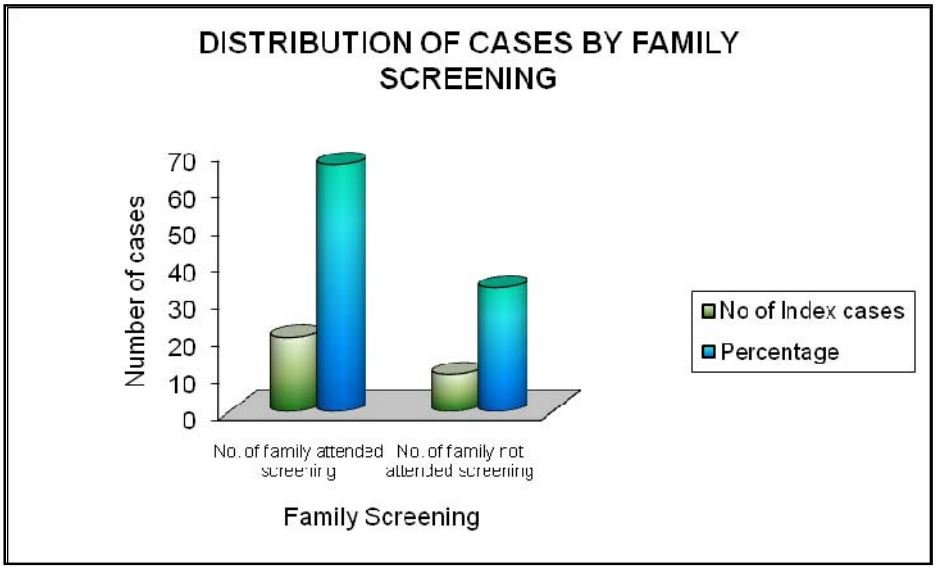
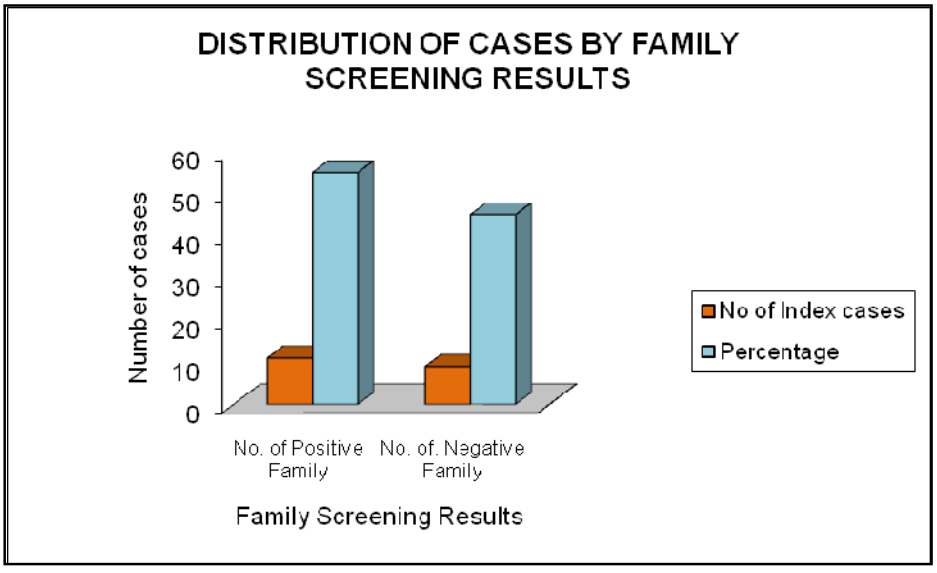


Table - 14

DISTRIBUTION OF CASES BY FAMILY SCREENING RESULTS

S. No	Family screening results	No of Index cases	Percentage
1	No. of Positive Family	11/20	55
2	No. of. Negative family	9/20	45

In this study 20 families attended screening. In this 20 families 11 (55%) families were found to the positive. 9 families (45%) were negative.



DISCUSSION

ADPKD is the most common inherited renal disease (Gasow, PA. Bennet WM, Breuning MH, Peter DJM).ADPKD affect approximately 500000 population in the united states and is the more frequent genetic cause of renal failure in adult accounting for 10% patient on dialysis in U.S (Torra 2008). The prevalence was1:500 – 1:1000(5).

As in any Autosomal Dominant disease, a patient with ADPKD has the defective gene on one of a pair of Autosomal chromosomes. Therefore, each offspring of an affected individual has a 50% chance of inheriting the chromosome carrying the defective gene and thus, inheriting the disease, ADPKD, which appeared clinically to be 1 entity of disease, actually results from at least 2 different gene defects. The most common gene, PKD_1, is located on the short arm of chromosome No.16. This discovery has made it possible for new methods to diagnose the disorder in gene carriers prior to the development of renal cysts. The location of the other gene, which has been called PKD2 or non- PKD1, is chromosome No. 4. The location of third gene (PKD 3) has not yet been determined. It appears that PKD1 accounts for approximately 90 percent of all ADPKD in the white population.[72] The disease arise from a spontaneous mutation[114]. The pathogenesis, of ADPKD is due to The Altered epithelial cell growth, secretion, and extracellular matrix

production have all been shown to contribute to the development of ADPKD[150]. These abnormalities could, in fact, contribute to cyst development and extrarenal manifestations.

Commonest age group of patients attending Nephrology and General Medicine OP/IP Dept were 51- 60 yrs age group of about (13 cases) 43% 41-50yrs age group were 8 cases (26.6%), 61-70 yrs age group were 3 cases, 21-30 yrs age group were 2 cases, 31-40 Yrs age group were 4 cases. The average age group of patient Attending OP/IP was 50.03 ± 11.4 (Mean ± SD).

That patients initial diagnosis were confirmed by 41-50 age group around 10 patients, 51-60 yrs age group around 9 patients, 61-70 yrs age group around 2 patients, 21-30yrs age group around 4 patients 31-40 yrs age group aground 5 patients.The average age at initial diagnosis in the study was 40.6 ± 18.8 (Mean ± SD) Range (24-65)

The average Age at initial diagnosis in the study was

40.6 ± 18.8 (Mean ± SD) Range 24-65

Dr. S.K HK et al 39.2 ± 13.8[118]

Dr. Alkis M. Pierides et al 1999 37.9 (Range 6-66 yrs) [119]

ADPKD may be revealed by renal symptoms. However, in a substantial number of cases, the disease is asymptomatic and is discovered during routine clinical examination, on abdominal

ultrasonography performed for extrarenal reasons, or during genetic investigation.

- Disease diagnosed by renal symptom

  In this study 19/30 (63%)

  Dr. S.K.Ha et al 15/30 (50%)[118].

- Disease diagnosed by Incidental finding

  In this study 7/30 (23.3%)

  Dr. S.K.Ha et al 8/30 (26.6%)[118]

- Disease diagnosed by uremic symptom

  In this study 4/30 (13.3%)

  Dr. S.K.Ha et al 2/30 (6.7%)[118].

Renal symptoms usually begin in the third or fourth decades. Common renal symptoms include flank or abdominal pain, palpable mass, haematuria, symptoms of renal infection and stones, and notcuria. Pain abdomen was reported in this study was 14/30 (46.6%) pain abdomen is the most frequent symptom reported by adult [45,46] Acute pain may be due to rend hemorrhage passage of stone , UTI, 3 patients presented with Renal calculus in this study this same 3 patients also presented with haematura, 9 patients presented with UTI, In this 9 patients, 6 patients were confirmed by positive urine culture and sensitivity. (In 5 Patients Urine E. coli grown 1 patient Klebsielle grown)

Renal calculus

In this study 3/30 (10%)

Dr. Alkis M. Pierides et al 1999, 4/105 (3.8%)[119]

Haematuria

In this study 3/30 (10%)

Dr. Alkis M. Pierides et al 1999 (12/105) (11.3%)[119]

UTI

In this study 9/30 (30%)

Dr. Alkis M. Pierides et al 1999 24/105 (22.6%)[119]

Uraemic symptoms

In is this study 4/30 (13.3%)

Dr. S.H.Ka et al 2/30 (6.7%)[118]

Hypertension is the most common cardiovascular manifestation, which occurs in about 70% of patients before the onset of renal insufficiency[115] Hypertension appears to be related to the renin-angiotensin system[116,117]. The rennin- angiotensin system is stimulated significantly more in hypertensive patients with ADPKD than in comparable patients with essential hypertension. The increased rennin release, perhaps due to renal ischemia cause by renal cyst expansion, contributes to the early development of hypertension in ADPKD.[117]

Hypertension

In this study	21/30 (70%)
Dr. S.H.Ka et al	22/30 (73.3%)[118]
Dr. Alkis M. Pierides et al 1999	24/105 (22.6%)[119]

Creatinine versus Hypertension

In this study

9 patients creatinine was <1.2 mg had HT, and 21 patients had creatinine ≥ 1.2 mg, In this 21 patients 12 patients had HT,

Dr. S.H Ka et al[118]

16 patients creatinine was <1.2 mgs, 9 patients had hyper tension 14 patients creatinine was ≥1.2 mgs, 13 patients had hyper tension

Clinically 5 cases found to be palpable renal mass by ballotable method. Other causes for palpable kidney are Diabetes mellitus early stage, amyloidosis multiple myeloma.

Cyst infection

3 cases (10%) presented with cyst infection uncomplicated cysts are echolucent. Complicated cysts exhibit a' complex pattern. This pattern is seen in cases with cyst infection, cyst haemorrhage (with or without cyst repture) or cyst calcification (usually is a residue after haemorrhage, but the possibility of calcification pointing to renal cell carcinoma should be kept in mind.

In the patient with ADPKD who complains of renal pain with or without macrohaematuria, one has to think of the following complications like cyst rupture, cyst hemorrhage, rupture of a bleeding cyst or bleeding from calyceal varicose, and rupture of the kidney (after blunt trauma). As soon as the patient has fever or signs of inflammation (e.g elevated CRP concentration), cyst infection should be suspected, which may require diagnostic puncture of a complicated cyst. Cyst infection is a medical emergency.

Extra renal manifestation was compared with Dr. S.H. Ka et al

Extra renal manifestation	**No.of patients in this study**	**Percentage**	**No.of patients Dr. S.H.Ka et al[118]**	**Percentage**
Liver cyst	4/30	13%	21/30	70%
Pancreatic cyst	1/30	3.3%	5/30	16.7%
Splenic cyst	-	-	2/30	6.6%
Diverticulosis	-	-	1/30	3.3%
Ovarian cyst	2/15	13.3	3/21	14.3
Uterine cyst	1/15	6.7	3/21	14.3%
Seminal vesicle cyst	1/15	6.7%	1/19	11.1%
Mitral valve prolapse	2/30	6.6%	5/30	16.7%

Anaemia was reported in this study was 9 patients (30%) oedema was reported in this study was 3 patients (10%).

Urine spot PCR was increased in 6 patients (20%). Proteinuria often used as a surrogate marker of disease activity in other kidney disorders, is usually <1 g/d. proteinuria, observed more frequently in those with large (mean combined renal volume 1190 ml) rather than small (578 ml) renal volumes, is also associated with a greater likelihood of a subsequent loss of renal function (9).

In index cases 5 patients founded to be CKD stage 1, 9 patients founded to be CKD stage 2, 7 patients founded to be in CKD stage 3 and 4. 2 patients founded to be CKD stage 5, but in the screened cases all cases (15 cases) found to be CKD stage 1.

The natural history of renal disease may occur as early as the first decade of life, or renal function may be well maintained into the eighth decade. Approximately 50% of patients had well preserved renal function at 70 years of age

Family Screening

Family screening is the screening method to detect the new cases, since ADPKD is familial diseases as a 50% chance of inheriting the chromosome carrying the defective gene and dose inheriting diseases. When we screen the family early, we can detect the disease early and delay the

morbidity and mortality due to ADPKD, Family History may be positive in this study was 11 cases (55%) out of 20 cases. 15(20%) cases were detected from 75 screened cases.

Positive Family History

In this study 11/20 (55%)

Dalgard 1957, Iglesias et al 1983 (60%) [119]

Dr. S.H Ka et al 6/30 (16.3%) [118]

Family screening was done in 20 patients out of 30 patients, from this 20 patients family I screened around 75 person. 10 patients family not attending family screening study. This is because of social stigma about the kidney diseases and lack of awareness about the disease. In this 20 families 11 families were positive, 9 families were negative. In this 11 families 15 cases were detected. In this 15 cases, 4 male and 11 female patients. Chances of female to female transmissions will be high, in this study because 9 screened female patients coming from female index cases. Since 15 cases, detected from 75 person the positivity is every 5th person in the family.

SUMMARY

Recently with the widespread use of new imaging techniques, the diagnosis of autosomal dominant polycystic kidney disease (ADPKD) is increasing. To analyses the extrarenal manifestation of ADPKD in Kilpauk Medical College Hospital retrospectively patients was studied the clinical characteristics of 30 patients with ADPKD. Thirty patients with ADPKD who had been diagnosed at Nephrology and General Medicini Department, Kilpauk Medical College Hospital. were recruited for this study. All patients past and family histories were re-evaluated, charts, ultrasound scan and CT scan were reviewed retrospectively. The male to female ratio was 15:15 in index cases, 4:11 in screened cases and the age of initial diagnosis was 40.6 ± 18.2 (Mean ±SD) years. In 19 cases (50%), ADPKD had been diagnosed by renal symptoms; in 7 cases (26.7%), by incidental finding like routine checkup, AN checkup, Infertility checkup, Master Health Checkup,post menopausal chekup and in 4 cases by Uremic symptoms in Index cases. Extrarenal involvement included Liver cysts (13.3% in index cases), (13.3% in screened case) and pancreatic cysts (3.3%), Ovarian cyst 6.7% in index cases, 6.7% in screened cases, uterine cyst 3.3 % in index cases 6.6% in screened cases seminal vesicle cyst 3.3%, index cases, Mitral valve prolapse 6.7% in index cases, 6.7% in screened cases Renal cysts are only one of a myriad of renal and extrarenal manifestation of ADPKD. ADPKD should be

managed systematically since this disorder is a systemic disease with clinically important involvement of the cardiovascular system, the gastrointestinal tract, the genitourinary system, and the musculoskeletal system. Family screening was done in 20 families out of 30 famiels. In this 20 families 11 families were positive, 9 families were Negative. In this 11 families 15 cases were detected. In this 15 cases 11 cases were children of patients. 4 cases were siblings of patients.

CONCLUSION

- In ADPKD , most common clinical presentation in 40's and 50's age group in this study
- ADPKD is higher in female the male in this study
- Pain abdomen and symptoms of UTI is the most common symptom
- Hypertension is the most common clinical presentation. ADPKD is known risk factors for renal failure, when it is associated with HT, it doubles the risk factors for renal failure.
- Liver Cyst is the most common extrarenal manifestation
- Mitral valve Prolapse is the most common extrarenal cardiovascular abnormality
- In this study 15 cases have been detected from 11 families.

STUDY LIMITATION

- Study population was small
- Family screening study was not able to do for all index cases, 20 cases were screened. For 10 case Screening could not be done .This is because of social stigma, and lack of awareness about the disease
- MRI was not done in the study to Rule out Berry aneurysm because of poor affordability
- Colonoscopy was not done in the study because of patients did not give consent for colonoscopy
- Follow up study was not done in this study.
- In this study I did not get exact proportion of ADPKD patients with family association

RECOMMENDATION

- In our country, genetic study is not possible, since USG in readily available and relatively inexpensive . So routine ultrasound scan to be done in all Hypertension, UTT symptom, and Pain abdomen to rule out ADPKD.
- Family screening to be done is all ADPKD Patients to delay and prevent morbidity and mortality due to ADPKD
- Follow up study to be done all ADPKD cases, to rule out disease progression.
- BP control, control of infection, Bed rest during Haematuria, Infection, pain abdomen, will delay progression of renal failure.

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PROFORMA

Serial No.

OP / IP No:

Name of the patient :

Age : Sex: M F

:

Address with phone No :

Socio Economic Status : Low Middle Higher

Education status : Below 12th Std Graduate

Post- Graduate

Occupation : Self Private Govt.

Cooly

Income per month : Below 2000 2001-5000

Above 5000

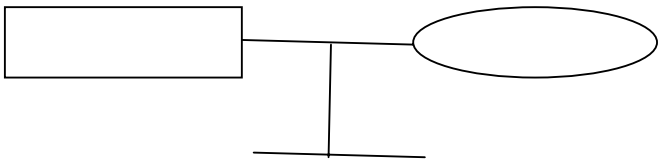
Urinary symptoms :

Duration :

Past History

	HT	Diabetes mellitus	Renal disease	TB	Others
Duration					

Family History



Personal History

	Smoking	Alcohol	Drug Abuse
Duration			

Total Dose

H/o. Drug Allergy : ☐ Yes ☐ No

Details ----------

Age at first time diagnosis :

Treatment & Dialysis details :

General Examination :

Build :

Nutrition :

Height :	
Weight :	BMI

Anemia	Lymph nodes	Jaundice	Cubbing	Cyanosis	Oedema

Temp pulse BP JVP

Abdomen

Cardiovascular system central Nervous System

Respiratory system Musculoskeletal system

Skin

ENT

Dental

Opthal

Investigations

- Urine Routine

  Date

  Date

- Urine culture and sensitivity :

- Urine Spot protein / : 1.

  Creatinine ratio

  2.

  24 hrs. urine protein

Date	Blood sugar	Blood urea	Serum creatinine	Na	K	Serum Proteins Albumin	Ca	PO4	Uric Acid	Cholesterol

Cock croft Gault formula : $\frac{140 - \text{Age} \times \text{IBW in (kg)}}{\text{Serum Creatinine} \times 72}$

(0.85 women)

CKD stage

CBC-TC ☐ DC ☐ Hb ☐ ESR ☐

- CT ☐ BT ☐ PT ☐
- ECG
- CXR
- Xray KUB
- USG Abdomen / Kidney and Urinary bladder
- Echo
- Analysis of Report

Signature of Guide

KEY WORDS

PKD_1	-	Poly Cystic Kidney Diseases 1
PKD_2	-	Poly Cystic Kidney Disease 2
ADPKD	-	Autosomal Dominant Polycystic Kidney Disease
HT	-	Hypertension
DM	-	Diabetis Mellitus
TB	-	Tuber culosis
ACE	-	Angiotensin Converting Enzyme
C_1AMP	-	Cylic Adenosine Monophosphate
EGF	-	Epidermal Growth factor
PLD	-	Polycystic Liver Disease
CKD	-	Chronic Kidney Disease
ECHO	-	EchoCardiogram
USG	-	Ultrasonography
CT	-	Computerised Tomography
UTI	-	Urinary Tract Infection
Urine RE	-	Urine Routeine Examination
Hb	-	Haemoglobin
OP/IP	-	Out Patient In Patient
Urine CXS	-	Urine Culture and Sensitivity

BP	-	Blood Pressure
ESRD	-	End Stage Renal Disease
CRISP Study	-	Consortium of Imaging Studies to assess the progression of Polyaystic Kidney
Nacl	-	Natrium Chloride
Urine Spot PCR	-	Protein creatinine Ratio
ICA	-	Intracerebral Artery
MVP	-	Mitral Valve prolapsed
MRI	-	Magnetic Resonance Imaging
ECG	-	Electrocardiogram
CKD	-	Chronic kidney disease
Alb	-	Albumin
TC	-	Total count
DC	-	Differential count
Bld	-	Blood
Dep	-	deposits
Epi	-	Epithelial cell
S.No	-	Serial Number